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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,128	09/20/2001	Andrew D. Murdin	032931-0252	9510

7590 06/09/2004

Bernhard D Saxe
Foley & Lardner
Suite 500
3000 K Street NW
Washington, DC 20007-5109

EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/857,128	MURDIN ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 2 sheets

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicants' amendment filed March 8, 2004 is acknowledged and has been entered. Claims 36-39 have been canceled. Claims 1-4, 8-14, 16, 18-22 and 27 have been amended. Claims 1-35 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment and/or comments with the exception of those discussed below.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 8-14 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 8-14 and 16 are vague and indefinite in the recitation of "capable of being expressed". It has been held that the recitation that an element is "capable of" performing a function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. *In re Hutchison*, 69 USPQ 138.

This rejection is maintained for the reasons of record. Applicant's arguments filed March 8, 2004 have been fully considered but they are not persuasive. Applicants have asserted a skilled person upon reading the specification understands that by "capable of being expressed" is meant that the nucleic acid is in an orientation and configuration required to produce the encoded polypeptide. This is a positive limitation indicating a limited number of orientation

and configuration; for example, if the nucleic acid is expressed out-of-frame, the polypeptide would not be produced as required. However, the claims should be definite in recited claim language. Applicants state that this phrase indicates a limited number of orientation and configuration; how many are there? Where is this defined in the specification?

4. Claims 8-14, 16, 27-32 and 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification appears to be enabled for a DNA vaccine for protecting against respiratory tract infection caused by *C. pneumoniae*. However, it is not clear which DNA encoding polypeptide was used. The specification states mice were immunized intramuscularly (i.m.) plus intranasally (i.n.) with plasmid DNA containing the coding sequence of a *C. pneumoniae* polypeptide. Was this SEQ ID NO: 5 or 6? Was the nucleic acid sequence that encodes the polypeptide of SEQ ID NO: 14 used? Further, the specification does not enable a DNA vaccine to protect against all Chlamydia infection (i.e. infection caused by *C. trachomatis*, *C. psittaci*, or *C. pecorum*). Will the *C. pnuemoniae*, assuming it is claimed SEQ ID NO: 14, protect against or treat infection caused by each one of these Chlamydia— *C. pneumoniae, C. trachomatis, C psittaci, C. pecorum*? What is the function of the polypeptide set forth in SEQ ID NO: 14? It is noted that there are differences in these chlamydial species. *C. trachomatis* and *C. pneumoniae* are both pathogens of humans but differ in their tissue tropism and spectrum of diseases. *C.*

pneumoniae is a newly recognized species of Chlamydia that is a natural pathogen of humans and causes pneumonia and bronchitis, while *C. trachomatis* infection causes trachoma, an ocular infection that leads to blindness, and sexually transmitted diseases such as PID, chronic pelvic pain, ectopic pregnancy and epididymitis (Kalman et al Nature Genetics, 1999, 21:385-389). Kalman et al teaches that analysis of the *C. pneumoniae* genome revealed 214 protein-coding sequences not found in *C. trachomatis*, most without homologous to other known sequences (Kalman et al p. 385). Although no function has been assigned to most of the unique *C. pneumoniae* genes, several have significant similarity to genes from other organisms (Kalman et al p. 388). Do any of the claimed sequences show similarity to genes known from other organisms? What is the function of the claimed protein? Further, the state of the art is unclear as to whether DNA vaccines are protective against Chlamydia infection. Svanholm et al (Scand. J. Immunol., 2000, 51:345-353) teaches that DNA vaccination using heat shock protein 60 gene of *C. pneumoniae* did not provide protection against challenge with *C. pneumoniae* in mice. However, if pIL-12 were administered there was increased protection of mice against infection with *C. pneumoniae* (abstract). Svanholm et al indicates that "[v]accines against *C. pneumoniae* have not been tested. Moreover, given the low DNA homology and different pathobiology of *C. pneumoniae* and *C. trachomatis*, different mechanisms or antigens may be involved in the protective vaccination." (p. 345, col. 2; see also Brunham et al, J. Infectious Diseases, 2000, 181/Suppl. 3:S538-S543). Penttila et al (Vaccine, 2001, 19:1256-1265) teaches that DNA immunization with *C. pneumoniae* genes coding for MOMP or phsp60 provided protection against *C. pneumoniae* challenge but pomp2 failed to protect against *C. pneumoniae* challenge (abstract). Penttila et

al indicates that the immunology of protection in *C. pneumoniae* infection is poorly understood, antibodies do not protect against *C. pneumoniae* challenge and that DNA vaccination offered no protection from pneumoniae (p. 1261, col. 1). Penttila et al also teaches an interesting difference between chlamydial species is related to the immunological role of MOMP. In *C. trachomatis*, MOMP is the immnodominant antigen, whereas in *C. pneumoniae* antibody responses only weakly target MOMP (p. 1262). Igietseme et al discusses the problems of chlamydia vaccines. "Despite considerable efforts and clinical and experimental evidence suggesting that at least partial protective immunity is feasible in humans, the development of reliable chlamydia vaccines using conventional immunization strategies have proven to be elusive. Among other setbacks, vaccine effectiveness was relatively limited because of poor immunogenicity; more importantly, the use of inactivated whole-chlamydia agents appears to be unattractive due to likely immunopathogenic components." (p. 6803). Saren et al (Infection and Immunity, 2002, 70/7:3336-3343) teaches that there is no vaccine against *C. pneumoniae* infection (abstract). Murdin et al (J. Infectious Diseases, 2000, 181/Suppl. 3:S552-S557) teaches that although considerable progress toward developing a *C. pneumoniae* vaccine has been made in the last 1-2 years, a true candidate vaccine does not yet exist (p. S554). "The development of a candidate vaccine requires the determination of both protective antigens and a safe, effective, formulation of those antigens." (p. S554). Murdin et al teaches that antigen formulation remains an area in which much information is still needed, including what constitutes a protective immune response to *C. pneumoniae* in humans, how to express recombinant antigens efficiently, and how to formulate them to elicit a protective response in humans (p. S554).

Applicants have indicated in the specification that C. trachomatis infection does not confer cross-immunity to *C. pneumoniae* (p. 3) and that there is no known effective vaccine for any human chlamydial infection (p. 6). The specification also indicates that many antigens recognized by immune sera to *C. pneumoniae* are conserved across all chlamydiae, but a 98, 76 and 54 kDa protein appear to be *C. pneumoniae*-specific (p. 7). The Summary of the Invention asserts that "[t]he present invention provides purified and isolated polynucleotide molecules that encode *Chlamydia* polypeptides which can be used in methods to prevent, treat, and diagnose *Chlamydia* infection." (p. 8). However, as set forth above the state of the art is unpredictable in that regard. Applicants have shown only one experiment of protection, using a DNA vaccine, but no other evidence of vaccine compositions comprising the polypeptide or antibody against the polypeptide or fusion proteins providing protection against *Chlamydia* infection. The specification is not enabled for vaccines that comprise an immunogenic fragment or for methods of detecting a Chlamydial infection. It is not clear from the specification that an immunogenic fragment is enabled, and what is meant by "which has been modified without loss of immunogenicity". In view of the state of the art it is not clear that vaccines as claimed by Applicants are feasible, or enabled.

The rejection is maintained for the reasons of record. Applicant's arguments filed March 8, 2004 have been fully considered but they are not persuasive. Applicants clarify that the passage beginning at page 17, line 19 to page 18, line 23, describing the immunization in mice and *C. pneumoniae* challenge, is a

prophetic description. This is made explicit by amendment of this passage to the present tense. The description now also makes clear which DNAs are to be used. The Examiner notes that in view of 3/8/04 amendment to the specification (pp. 17-18) from the past to the present tense the enablement is not understood. The specification is now totally prophetic. What enablement with regard to the DNA vaccines or vaccine vectors and polypeptide vaccines was established at the time of filing of the present application? There does not appear to be any examples set forth in the specification to established vaccine protection against *Chlamydia* infection in a subject using the claimed nucleic acid sequences of SEQ ID NO: 5 or 6 in a vaccine vector or the amino acid sequence of SEQ ID NO: 14 in polypeptide vaccine. Applicants have asserted that the invention as claimed does not recite protection against all *Chlamydia*. However, the claims are directed to a vaccine vector or vaccine, and the specification teaches that the compositions (i.e. vaccines) can be administered to the mammal in an immunogenically effective amount of a polypeptide of the invention to elicit a protective immune response to *Chlamydia* and particularly, preventing and/or treating a *Chlamydia* (e.g. *C trachomatis, C. psittaci, C. pneumoniae,* or *C. pecorum*) infection, by administering a prophylactic or therapeutic amount of a polypeptide of the invention to an infected individual. Additionally the seventh aspect of the invention encompasses the use of a polypeptide of the invention in the preparation of a medicament for preventing and/or treating *Chlamydia* infection. (see pp. 39-40). The claims, read broadly, and in view of the specification encompass providing protection against all *Chlamydia* infections. The claims, vaccine vectors or vaccines, do not recite a specific type of *Chlamydia* infection. Further, the specification at page 47 defined protection "...shown when infection is reduced

by comparison to the control group. Such an evaluation is made for polynucleotides, vaccine vectors, polypeptides and derivatives thereof, as well as antibodies of the invention." (p. 47, l. 9-12). The specification has adopted the normal meaning of the term vaccine (i.e. to provide protection against infection). Even though the specification states this, there is no enablement for these vaccines and in view of the state of the art that vaccines to protect against *Chlamydia* infection has not been achieved and is difficult (see pp. 4-6 of this actions) there would be undue experimentation involved to practice the claimed invention.

The Murdin Declaration under 37 CFR 1.132 filed March 8, 2004 is insufficient to overcome the rejection of claims 8-14, 16, 27-32 and 34 based upon 112, first paragraph lack of enablement as set forth in the last Office action. Applicants have asserted that the claimed sequences do confer immunoprotection and that the invention is fully enabled. Attached is a Declaration under 37 CFR 1.132 of inventor Andrew Murdin. The declaration describes experiments performed by the assignee, Aventis Pasteur, which demonstrate that mice immunized with a nucleic acid encoding SEQ ID NO:14 are protected from a subsequent challenge with *C. pneumoniae*. Details of the experiments performed are *essentially identical* to the description on page 17, line 19 to page 18, line 23.

Are the procedures described in the declaration the same or not? What are the differences in procedures since Applicants state that they are *essentially identical*? In order for a declaration to provide support for enablement of the claimed invention the results/data shown in the declaration have to have been performed by the exact same (i.e. identical) procedure as described in the filed specification. It is not clear what was done in this situation since Applicants have amended (3/8/04) the specification to read prophetically and the Murdin

declaration states that the details of the experiments performed are *essentially identical* to the description on page 17, line 19 to page 18, line 23.

5. Claims 1-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Griffais et al (6559294).

Griffais et al discloses the nucleic acid sequences as claimed by Applicants (abstract; col. 12, l. 28-54; see claims). The prior art SEQ ID NO: 1 discloses SEQ ID NO: 5 and 6. Griffais et al discloses the amino acid sequence of SEQ ID NO: 14, see SEQ ID NO: 472 of the issued patent (see col. 27 and sequence listing). The prior art discloses the genomic sequence and the nucleotide sequences encoding polypeptides of C. pneumoniae (abstract). Griffais et al discloses vectors including the said sequences and cells or animals transformed with these vectors (cols. 45-48; claims), methods of producing polypeptides (cols. 50-51; claims), fusion proteins (col. 48-49), antisense molecules (col. 49), antibodies (col. 52; col. 54), methods of detection (using nucleic acids, polypeptides or antibodies) and kits for diagnosing Chlamydia infection (cols. 52-53, 55, 58, 59), primers and probes (cols. 57-58), as well as vaccine and pharmaceutical compositions (col. 61-64) for prevention and/or treatment of Chlamydia infection (abstract). Griffais et al discloses a fragment of at least 5 amino acids of a polypeptide as well as a modified polypeptide (col. 13, l. 43-48; col. 15; col. 27).

It is noted that products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art discloses the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

The prior art anticipates the claimed invention. Since the Patent Office does not have the facilities for examining and comparing applicants' DNA, proteins, vaccines, compositions, and methods with the DNA, proteins, vaccines, compositions and methods of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed DNA, proteins, vaccines, compositions, and methods with the DNA, proteins, vaccines, compositions and methods of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

The rejection of claims 1-35 under 35 U.S.C. § 102(e) as anticipated by Griffais et al (6449294) is maintained. This rejection is maintained for essentially the same reasons as the rejection of claims 1-39 under this statutory provision, as set forth in the last Office action. Applicants' arguments filed March 8, 2004, have been fully considered but they are not deemed to be persuasive. The Murdin Declaration filed on March 8, 2004 under 37 CFR 1.131 has been considered but is ineffective to overcome the 102(e) reference of Griffias et al. It is noted that the declaration has been signed by only one of the inventors (Murdin). All inventors have not signed the declaration. It is not clear why Dathao Ho signed one of the pages of data provided in the declaration. Dathao Ho did not swear behind the date in the proper manner. Dathao Ho is not one of the inventors. Further, paragraph 4 of the declaration states "CPN100638 corresponds to the gene identified as SEQ ID Nos: 5, 6 and 14 of the application. The amino acid sequence of CPN100638 set forth in the attached document is identical to SEQ ID No: 14 of this application. The sequences and restriction map are *essentially the same* as Figures 5 and 6 of

the application." Are they the same, and if not what are the differences? This does not emphatically state that the data in the declaration and that the sequences found in the specification are the exact it and as a result Applicants were in possession of the sequences prior to November 4, 1998.

6. No claims are allowed.

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is

571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
June 3, 2004